

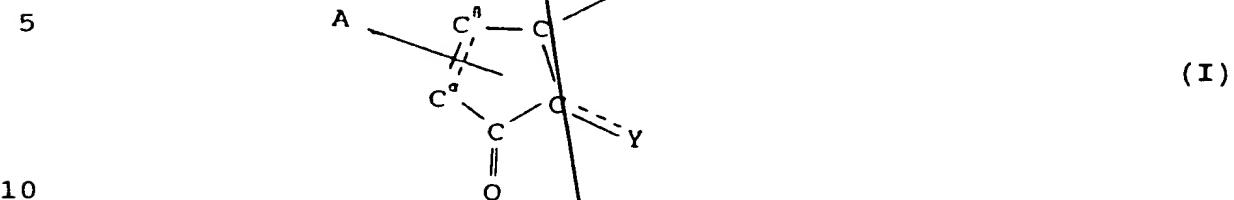
That which is claimed is:

1. A method for modulating process(es) mediated by peroxisome proliferator activated receptor-gamma (PPAR- γ), said method comprising conducting said process(es) in the presence of at least one PPAR- γ -selective prostaglandin or prostaglandin-like compound or precursor thereof.

2. A method according to Claim 1 wherein said PPAR- γ -selective prostaglandin is selected from a prostaglandin-J₂, a prostaglandin-D₂, or a precursor thereof.

3. A method according to Claim 2 wherein said prostaglandin-J₂ is selected from prostaglandin-J₂, Δ^{12} -prostaglandin-J₂ or 15-deoxy- $\Delta^{12,14}$ -prostaglandin-J₂.

4. A method according to Claim 1, wherein said PPAR- γ -selective prostaglandin or prostaglandin-like compound has the structure I:



wherein:

15 A is selected from hydrogen or a leaving group at the α - or β - position of the ring, or A is absent when there is a double bond between C $^{\alpha}$ and C $^{\beta}$ of the ring;

X is an alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl or

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substituted alkynyl group having in the range of 2 up to 15 carbon atoms; and Y is an alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl or substituted alkynyl group having in the range of 2 up to 15 carbon atoms.

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5. A method according to claim 4 wherein:

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X of Formula I is selected from:

-(CRR)_m-Z,
-(CRR)_{m'}-C(R)=C(R)-(CRR)_m-Z, or
-(CRR)_{m''}-C≡C-(CRR)_{m''}-Z, wherein:
each R is independently selected from hydrogen, lower alkyl, substituted lower alkyl, hydroxy, lower alkoxy, thioalkyl, halogen, trifluoromethyl, cyano, nitro, amino, carboxyl, carbamate, sulfonyl or sulfonamide,
m falls in the range of 1 up to 15,
each m' falls independently in the range of 0 up to 12, with the proviso that the total chain length of the alkenyl moiety does not exceed 15 carbon atoms,
each m'' falls independently in the range of 0 up to 12, with the proviso that the total chain length of the alkynyl moiety does not exceed 15 carbon atoms, and
Z is a polar, heteroatom-containing substituent; and

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Y of Formula I is selected from:

=C(R)-[C(R)=C(R)]_n-(CRR)_{n'}-Z' (II),

=C(R)-[C≡C]_{n''}-(CRR)_{n'}-Z' (IIA),

=C(R)-CRR-CR(R')-(CRR)_{n'}-Z' (III),

-[C(R)=C(R)]_n-(CRR)_{n'}-Z' (IV),

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-[C≡C]_n-(CRR)_{n'}-Z' (IVA),

wherein

each R is independently as defined above,

each R' is independently selected

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from H, lower alkyl, substituted lower alkyl, or a leaving group,

Z' is selected from H, lower alkyl or substituted lower alkyl,

n falls in the range of 0 up to 4,

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n' falls in the range of 2 up to 12, and

n'' falls in the range of 1 up to 3.

6. A method according to claim 5 wherein Z is selected from cyano, nitro, amino, carbamate, or a substituent having the structure:

-CH₂OR', wherein R' is selected from H, alkyl, alkenyl, alkynyl, acyl or aryl;

-C(O)R'', wherein R'' is selected from H, alkyl, substituted alkyl, alkoxy, alkylamino, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, aryloxy, arylamino, alkylaryl, substituted alkylaryl, arylalkyl, substituted arylalkyl, heterocyclic, substituted heterocyclic or trifluoromethyl,

-CO₂R''', wherein R''' is selected from H, alkyl, alkenyl or alkynyl;

-SR', -S(O)R', -S(O)₂R' or -S(O)₂NHR', wherein each R' is as defined above.

7. A method according to claim 5 wherein:

X of Formula I is $-\text{CRR}-\text{C}(\text{R})=\text{C}(\text{R})-(\text{CRR})_m-\text{Z}$,
wherein:

5 each R is independently selected from
hydrogen, lower alkyl, substituted
lower alkyl, hydroxy, alkoxy (of a
lower alkyl group), halogen,
trifluoromethyl, amino, carboxyl, or
sulfonyl,

10 m falls in the range of 1 up to 6, and
Z is selected from $-\text{CH}_2\text{OH}$, $-\text{CH}_2\text{OAc}$, $-\text{CO}_2\text{H}$,
 $-\text{CO}_2\text{Me}$ or $-\text{CO}_2\text{Et}$; and

15 Y of Formula I is selected from:

$=\text{C}(\text{R})-\text{C}(\text{R})=\text{C}(\text{R})-(\text{CRR})_{n'}-\text{Z}'$ (II),

$=\text{C}(\text{R})-\text{CRR}-\text{CR}(\text{R}')-(\text{CRR})_{n'}-\text{Z}'$ (III), or

20 $-\text{C}(\text{R})=\text{C}(\text{R})-\text{CR}(\text{R}')-(\text{CRR})_{n'}-\text{Z}'$ (IV), wherein
each R is independently as defined
above,

each R' is independently selected
from H, lower alkyl, substituted
lower alkyl, or a leaving group,
Z' is selected from H, lower alkyl or
substituted lower alkyl, and
n' falls in the range of 1 up to 6.

25 8. A method according to claim 7 wherein Y of
Formula I is

$=\text{C}(\text{R})-\text{C}(\text{R})=\text{C}(\text{R})-(\text{CRR})_{n'}-\text{Z}'$ (II),

wherein each R is selected from hydrogen, lower alkyl or

5 substituted lower alkyl, n is 1, n' falls in the range of
about 2 up to 6, and Z' is selected from hydrogen or
lower alkyl.

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9. A method according to claim 7 wherein Y of Formula I is

$$=C(R)-CRR-CR(R')-(CRR)_{n'}-Z' \text{ (III) or}$$
$$-C(R)=C(R)-CR(R')-(CRR)_{n'}-Z' \text{ (IV),}$$

5 wherein each R is selected from hydrogen, lower alkyl or substituted lower alkyl, R' is selected from hydrogen, lower alkyl, or an hydroxy group, n is 1, n' falls in the range of about 2 up to 6, and Z' is selected from hydrogen or lower alkyl.

10. A method according to claim 5 wherein A is 9-OH, Y is IV, each R is hydrogen, R' is hydroxy, Z is $-CO_2H$, m = 3, Z' is methyl, n = 1 and n' = 4.

11. A method according to claim 5 wherein A is absent, Y is IV, each R is hydrogen, R' is hydroxy, Z is $-CO_2H$, m is 3, Z' is methyl, n = 1 and n' = 4.

12. A method according to claim 5 wherein A is absent, Y is II, each R is hydrogen, R' is hydroxy, Z is $-CO_2H$, m = 3, Z' is methyl, n = 1 and n' = 4.

13. A method according to claim 5 wherein A is absent, Y is I, each R is hydrogen, Z is $-CO_2H$, m = 3, Z' is methyl, n = 1 and n' = 4.

14. A method according to claim 1 wherein said process mediated by PPAR- γ is cell differentiation to produce lipid-accumulating cells.

15. A method according to claim 1 wherein said process mediated by PPAR- γ is the response of the recipient to insulin.

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16. A method of testing a compound for its ability to regulate transcription-activating effects of a peroxisome proliferator activated receptor-gamma (PPAR- γ), said method comprising assaying for changes in 5 the level of reporter protein present as a result of contacting cells containing said receptor and reporter vector with said compound;

wherein said reporter vector comprises:

10 (a) a promoter that is operable in said cell,
(b) a hormone response element, and
(c) a DNA segment encoding a reporter protein,

15 wherein said reporter protein-encoding DNA segment is operatively linked to said promoter for transcription of said DNA segment, and

20 wherein said hormone response element is operatively linked to said promoter for activation thereof.

17. A method according to Claim 16 wherein said hormone response element is a direct repeat of two or more half sites separated by a spacer of one nucleotide, wherein said spacer can be A, C, G or T, 5 wherein each half site comprises the sequence

-RGBNNM-,

wherein

10 R is selected from A or G;

B is selected from G, C, or T;

each N is independently selected from

A, T, C, or G; and

M is selected from A or C;

15 with the proviso that at least 4 nucleotides of said -RGBNNM- sequence are identical with the nucleotides at corresponding positions of the sequence -AGGTCA-; and

wherein said response element is optionally preceded by N_x , wherein x falls in the range of 0 up to 5.

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18. A method according to claim 17 wherein said response element has at least one copy of the minimal sequence:

AGGACA A AGGTCA,

5 wherein said minimal sequence is optionally flanked by additional residues.

19. A method according to claim 17 wherein said response element has at least one copy of the sequence:

GGACC AGGACA A AGGTCA CGTTC.

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20. A method according to claim 16 wherein said compound is a putative antagonist for said peroxisome proliferator activated receptor-gamma, and wherein said contacting is carried out in the presence of

5 increasing concentrations of said compound, and

a fixed concentration of at least one agonist for said peroxisome proliferator activated receptor-gamma.

21. A method according to Claim 16 wherein said contacting is carried out in the further presence of at least one PPAR- γ -selective modulator.

22. A method for preventing obesity, said method comprising administering to a subject in need thereof an amount of a peroxisome proliferator activated receptor-gamma (PPAR- γ) antagonist effective to block

5 cell differentiation to produce lipid-accumulating cells.

23. A method for treating diabetes, said method comprising administering to a subject in need thereof an amount of a peroxisome proliferator activated receptor-gamma (PPAR- γ) agonist effective to lower the 5 blood glucose level of said subject.



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